CLAIMS

1. A composition comprising a T-cell receptor (TCR) that specifically binds to a mutant RAS (mRAS) peptide in the context of HLA-A*11:01, wherein the HLA-A*11:01 molecule comprises at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 5-12; wherein the TCR comprises

(a) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 12-1 (TRAV12-1) CDR1 comprising the amino acid sequence of SEQ ID NO: 31, TRAV12-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 32, TRAV12-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 33, T cell receptor beta variable 28 (TRBV28) CDR1 comprising the amino acid sequence of SEQ ID NO: 37, TRBV28 CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and TRBV28 CDR3 comprising the amino acid sequence of SEQ ID NO: 39;

b) the TCR comprises TRAV12-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 31, TRAV12-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 32, TRAV12-1 CD3 comprising the amino acid sequence of SEQ ID NO: 33, TRBV28 CDR1 comprising the amino acid sequence of SEQ ID NO: 37, TRBV28 CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and TRBV28 CDR3 comprising the amino acid sequence of SEQ ID NO: 39;

c) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 17 (TRAV17) CDR1 comprising the amino acid sequence of SEQ ID NO: 45, TRAV17 CDR2 comprising the amino acid sequence of SEQ ID NO: 46, TRAV17 CDR3 comprising the amino acid sequence of SEQ ID NO: 47, T cell receptor beta variable 11-2 (TRBV11-2) CDR1 comprising the amino acid sequence of SEQ ID NO: 50, TRBV11-2 CDR2 comprising the amino acid sequence of SEQ ID NO: 51, and TRBV11-2 CDR3 comprising the amino acid sequence of SEQ ID NO: 52;

(d) the TCR comprises TRAV17 CDR1 comprising the amino acid sequence of SEQ ID NO: 45, TRAV17 CDR2 comprising the amino acid sequence of SEQ ID NO: 46, TRAV17 CDR3 comprising the amino acid sequence of SEQ ID NO: 47, TRBV11-2 CDR1 comprising the amino acid sequence of SEQ ID NO: 50, TRBV11-2 CDR2 comprising the amino acid sequence of SEQ ID NO: 51, and TRBV11-2 CDR3 comprising the amino acid sequence of SEQ ID NO: 52;

(e) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 39 (TRAV39) CDR1 comprising the amino acid sequence of

SEQ ID NO: 17, TRAV39 CDR2 comprising the amino acid sequence of SEQ ID NO: 18, TRAV39 CDR3 comprising the amino acid sequence of SEQ ID NO: 19, T cell receptor beta variable 20-1 (TRBV20-1) CDR1 comprising the amino acid sequence of SEQ ID NO: 23, TRBV20-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 24, and TRBV20-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 25; or

(f) the TCR comprises TRAV39 CDR1 comprising the amino acid sequence of SEQ ID NO: 17, TRAV39 CDR2 comprising the amino acid sequence of SEQ ID NO: 18, TRAV39 CDR3 comprising the amino acid sequence of SEQ ID NO: 19, TRBV20-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 23, TRBV20-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 24, and TRBV20-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 25; or

(g) the composition comprises a fusion polypeptide comprising a TCR α chain and a TCR β chain.

2. The composition of claim 1, wherein the RAS peptide comprises a mutation at a position corresponding to G12 relative to wildtype RAS.

3. The composition of claim 1, wherein the mutation of the mRAS peptide corresponds to a mutation selected from the group consisting of G12C, G12D, G12R, and G12V; relative to wildtype RAS.

4. The composition of claim 1, wherein the TCR comprises TRAV39 CDR1 comprising the amino acid sequence of SEQ ID NO: 17, TRAV39 CDR2 comprising the amino acid sequence of SEQ ID NO: 18, TRAV39 CDR3 comprising the amino acid sequence of SEQ ID NO: 19, TRBV20-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 23, TRBV20-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 24, and TRBV20-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 25.

5. The composition of claim 1, wherein the TCR comprises TRAV12-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 31, TRA V12-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 32, TRAV12-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 33, TRBV28 CDR1 comprising the amino acid sequence of SEQ ID NO: 37, TRBV28 CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and TRBV28 CDR3 comprising the amino acid sequence of SEQ ID NO: 39.

6. The composition of claim 1, wherein the TCR comprises TRAV17 CDR1 comprising the amino acid sequence of SEQ ID NO: 45, TRAV17 CDR2 comprising the amino acid sequence of SEQ ID NO: 46,

TRAV17 CDR3 comprising the amino acid sequence of SEQ ID NO: 47, TRBV11-2 CDR1 comprising the amino acid sequence of SEQ ID NO: 50, TRBV11-2 CDR2 comprising the amino acid sequence of SEQ ID NO: 51, and TRBV11-2 CDR3 comprising the amino acid sequence of SEQ ID NO: 52.

7. The composition of claim 1, wherein the composition comprises a fusion polypeptide comprising a TCR a chain and a TCR β chain.

8. The composition of claim 7, wherein the fusion polypeptide comprises a linker domain.

9. The composition of claim 8, wherein the linker domain is a cleavable linker domain.

10. A composition comprising an isolated nucleic acid molecule encoding a composition of any one of claims 1-9.

11. A cell modified to express a T-cell receptor (TCR) that specifically binds to a mutant RAS (mRAS) peptide in the context of HLA-A*11:01, wherein the HLA-A*11:01 molecule comprises at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 5-12;

wherein the cell is an immune cell is selected from the group consisting of a T cell, NK cell, and NK T cell;

wherein the TCR comprises

(a) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 12-1 (TRAV12-1) CDR1 comprising the amino acid sequence of SEQ ID NO: 31, TRAV12-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 32, TRAV12-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 33, T cell receptor beta variable 28 (TRBV28) CDR1 comprising the amino acid sequence of SEQ ID NO: 37, TRBV28 CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and TRBV28 CDR3 comprising the amino acid sequence of SEQ ID NO: 39;

b) the TCR comprises TRAV12-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 31, TRAV12-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 32, TRAV12-1 CD3 comprising the amino acid sequence of SEQ ID NO: 33, TRBV28 CDR1 comprising the amino acid sequence of SEQ ID NO: 37, TRBV28 CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and TRBV28 CDR3 comprising the amino acid sequence of SEQ ID NO: 39;

c) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 17 (TRAV17) CDR1 comprising the amino acid sequence of SEQ ID NO: 45, TRAV17 CDR2 comprising the amino acid sequence of SEQ ID NO: 46, TRAV17 CDR3 comprising the amino acid sequence of SEQ ID NO: 47, T cell

receptor beta variable 11-2 (TRBV11-2) CDR1 comprising the amino acid sequence of SEQ ID NO: 50, TRBV11-2 CDR2 comprising the amino acid sequence of SEQ ID NO: 51, and TRBV11-2 CDR3 comprising the amino acid sequence of SEQ ID NO: 52;

(d) the TCR comprises TRAV17 CDR1 comprising the amino acid sequence of SEQ ID NO: 45, TRAV17 CDR2 comprising the amino acid sequence of SEQ ID NO: 46, TRAV17 CDR3 comprising the amino acid sequence of SEQ ID NO: 47, TRBV11-2 CDR1 comprising the amino acid sequence of SEQ ID NO: 50, TRBV11-2 CDR2 comprising the amino acid sequence of SEQ ID NO: 51, and TRBV11-2 CDR3 comprising the amino acid sequence of SEQ ID NO: 52;

(e) the TCR comprises at least one CDR selected from the group consisting of: T cell receptor alpha variable 39 (TRAV39) CDR1 comprising the amino acid sequence of SEQ ID NO: 17, TRAV39 CDR2 comprising the amino acid sequence of SEQ ID NO: 18, TRAV39 CDR3 comprising the amino acid sequence of SEQ ID NO: 19, T cell receptor beta variable 20-1 (TRBV20-1) CDR1 comprising the amino acid sequence of SEQ ID NO: 23, TRBV20-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 24, and TRBV20-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 25; or

(f) the TCR comprises TRAV39 CDR1 comprising the amino acid sequence of SEQ ID NO: 17, TRAV39 CDR2 comprising the amino acid sequence of SEQ ID NO: 18, TRAV39 CDR3 comprising the amino acid sequence of SEQ ID NO: 19, TRBV20-1 CDR1 comprising the amino acid sequence of SEQ ID NO: 23, TRBV20-1 CDR2 comprising the amino acid sequence of SEQ ID NO: 24, and TRBV20-1 CDR3 comprising the amino acid sequence of SEQ ID NO: 25; or

(g) the composition comprises a fusion polypeptide comprising a TCR α chain and a TCR β chain.

12. The cell of claim 11, wherein the mRAS peptide comprises a mutation at a position corresponding to G12 relative to wildtype RAS.

13. The cell of claim 12, wherein the mutation of the mRAS peptide corresponds to a mutation selected from the group consisting of G12C, G12D, G12R, and G12V; relative to wildtype RAS.

14. The cell of claim 11, wherein the cell is modified to express a fusion polypeptide comprising a TCR alpha chain and a TCR beta chain.

15. The cell of claim 11, wherein the cell is genetically modified by introduction of an isolated nucleic acid molecule encoding a polypeptide comprising at least one of: a TCR alpha chain and a TCR beta chain.

16. The cell of claim 11, wherein the cell is autologous to a subject having a cancer associated with RAS.

17. The cell of claim 11, wherein the cell is autologous to a subject having a HLA type selected from the group consisting of: HLA-A*02:01, HLA-A*03:01, HLA-A*11:01, and HLA-B*07:02.

18. A medicament for treating a cancer associated with mRAS in a subject in need thereof, the medicament comprising the cell of any one of claims 11-17.

19. The medicament of claim 18, wherein the cancer associated with mRAS is selected from the group consisting of pancreatic cancer, pancreatic ductal adenocarcinoma (PDA), colon cancer, colorectal adenocarcinoma, myeloma, multiple myeloma, lung adenocarcinoma, melanoma, uterine cancer, thyroid cancer, acute myelogenous leukemia (AML), urothelial cancer, gastric adenocarcinoma and cervical adenocarcinoma, head and neck squamous cell carcinoma (SCC), Diffuse large B-cell lymphoma (DLBCL), esophageal adenocarcinoma, Chronic lymphocytic leukemia (CLL), lung SCC, small cell lung cancer (SCLC), renal papillary cancer, Hepatocellular carcinoma (HCC), breast cancer, cervical SCC, ovarian adenocarcinoma, adrenal cancer, prostate cancer, neuroblastoma, glioblastoma multiforme (GBM), medulloblastoma, Renal cell carcinoma (RCC), esophageal SCC, osteosarcoma, sarcoma, and small intestine neuroendocrine tumor (NET).

20. The medicament of claim 18, wherein the subject has an identified HLA type.

21. The medicament of claim 18, wherein the medicament comprises one or more cells of the subject that is isolated and modified to express the TCR.

22. The medicament of claim 18, wherein the medicament comprises one or more cells modified to express the TCR by contacting the one or more cells with an isolated nucleic acid molecule that encodes one or more of: a TCR alpha chain and a TCR beta chain.